K 013169

APR 0 2 2002

March 21, 2002

510(K) SUMMARY

Cylex Inc. Immune Cell Function Assay

Submitted by:

Cylex Inc.
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Contact: Dr. Judy Britz

Name of Device:

Trade Name: Immune Cell Function Assay
Common Name: CD4 Cell Stimulation Assay
Classification Name: Automated Differential Cell Counter

Predicate Device: Becton Dickinson TriTest™ CD4 FITC/CD8 PE/CD3 PerCP Reagent;
Becton Dickinson MultiTest™ CD3 FITC/CD8 PE/CD45 PerCP/CD4 APC Reagent

Device Description:
Intended Use: The **Cylex Immune Cell Function Assay** measures the concentration of ATP from circulating CD4 cells following *in vitro* stimulation with phytohemagglutinin (PHA) as an indicator of immune cell function. This measurement is made on heparin anti-coagulated whole blood using a luminometer and luciferin/luciferase. The assay is used for the detection of cell mediated immune response in populations undergoing immunosuppressive therapy for organ transplant.

Test Description: The **Cylex Immune Cell Function Assay** detects cell-mediated immunity in whole blood after a 15-18 hour incubation with stimulant. During incubation, increased ATP synthesis occurs within the cells that respond to the stimulant phytohemagglutinin (PHA). Concurrently, whole blood is incubated in the absence of stimulant for the purpose of assessing basal ATP activity. Anti-CD4 monoclonal antibody coated magnetic particles are added to immunoselect CD4 cells from both the stimulated and non-stimulated wells. After washing the selected CD4 cells on a magnet tray, Lysis Reagent is added to release intracellular ATP. Addition of Luminescence Reagent (luciferin/luciferase) to the released ATP produces light according to the following equation:

$$\text{Luciferin} + \text{ATP} + O_2 \xrightarrow[\text{Luciferase}]{Mg^{2+}} \text{Oxyluciferin} + \text{AMP} + \text{Pyrophosphate} + CO_2 + \text{Light}$$

The amount of light measured by a luminometer (emission maximum 562 nm) is proportional to the concentration of ATP. The concentration of ATP (ng/mL) is calculated from a calibration curve and compared to ATP level ranges to characterize the cellular immune function of the sample.

Substantial Equivalence:

The **Cylex Inc. Immune Cell Function Assay** has been found to be substantially equivalent to the Becton Dickinson TriTest™ CD4 FITC/CD8 PE/CD3 PerCP Reagent (K971205) and MultiTest™ CD3 FITC/CD8 PE/CD45 PerCP/CD4 ACP Reagent (K974360). All assays differentiate CD4 cells; the Cylex assay determines the responsiveness of those cells and the Becton Dickinson assays count the number of those cells.

A multi-center study was conducted on freshly drawn blood collected from 44 apparently healthy adults and 78 transplant recipients (17 at discharge from the hospital and 61 post-discharge follow-up). The samples were evaluated with the Cylex Immune Cell Function Assay. The apparently healthy adult population consisted of 11% (5) females, 86% (38) males and 3% (1) unknown, with an age range of 20 - 60 years. The ethnicity of the population was 80% (35) African American, 16% Caucasian (7), and 4% (2) other or unknown. The transplant population consisted of 33% (26) females and 67% (52) males, with an age range of 20 - 64 years. The ethnicity of the population was 15% (12) African American, 74% Caucasian (58), 10% (8) other or unknown. The organs transplanted were 55% (43) liver, 36% (28) kidney, 4% (3) pancreas, and 5% (4) multiple organs.

For purposes of these calculations, samples with %CV > 20% (after application of the outlier rule) were not included. The means of the two populations were found to be statically different; the results are summarized in the following table.

Summary of Clinical Trial Results

Population	Statistic	Cylex ICF Assay (ATP ng/mL)	Comparator Assay CD4 Count by Flow Cytometry (cells/μL)
Apparently Healthy (Non-immunosuppressed)	n	40	40
	Mean	464	746
	SD	145	431
	Median	443	654
	Range of Values	243-967	130-2659
Transplant (immunosuppressed)	n	63	63
	Mean	304	542
	SD	163	423
	Median	293	503
	Range of Values	58-759	<68*-1904

*Lower linear limit of the flow cytometry assay

NOTE: The means of the Cylex ICF Assay results for the two populations are statistically significantly different ($p < 0.0001$). The means of the comparator assay CD4 count results for the two populations are also statistically significantly different ($p < 0.0001$).

Cylex Inc. Immune Cell Function Assay (cont.)

Cylex ICF Assay Result	Patient Status		Total
	Transplant Subjects	Apparently Healthy Adults	
≤225 ATP ng/mL	24 (38%)	0 (0%)	24
226 - 524 ATP ng/mL	33 (52%)	27 (67%)	60
≥525 ATP ng/mL	6 (10%)	13 (33%)	19
Total	63	40	103

Total CD4 Count	Patient Status		Total
	Transplant Subjects	Apparently Healthy Adults	
<410 cells/μL	29 (46%)	8 (20%)	37
≥410 cells/μL	34 (54%)	32 (80%)	66
Total	63	40	103

The percentage of transplant patients with an assay result <525 ATP ng/mL was 90% (57/63, 95% confidence interval 80.4 – 96.4%). The percentage of transplant subjects having an assay result ≤225 ATP ng/ml was 38% (24/63, 95% confidence interval 26.1 – 51.2%). The percentage of transplant subjects having an assay result ≥525 ATP ng/mL was 10% (6/63, 95% confidence interval 3.6 – 19.6%).

The percentage of apparently healthy adults having an assay result <525 ATP ng/mL was 67% (27/40, 95% confidence interval 50.9 – 81.4%). The percentage of apparently healthy adults having an assay result ≤225 ATP ng/mL was 0%. The percentage of apparently healthy adults having an assay result ≥525 ATP ng/mL was 33% (13/40, 95% confidence interval 18.6 – 49.1%).

*U.S. Patent No. 5,773,232

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Cylex Inc.
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APR 0 2 2002

Re: K013169
Trade/Device Name: Cylex Immune Cell Function Assay
Regulation Number: 21 CFR 864.5220
Regulation Name: Automated Differential Cell Counter
Regulatory Class: Class II
Product Code: NID
Dated: January 14, 2002
Received: January 15, 2002

Dear Ms Smith:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsma/dsmamain.html".

Sincerely yours,

Steven Gutman

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical Laboratory-Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

510(k) Number (if known): K013169

Device Name: Immune Cell Function Assay

Indications For Use:

The **Cylex Immune Cell Function Assay** detects cell-mediated immunity (CMI) by measuring the concentration of ATP from CD4 cells following stimulation. This measurement is made on heparin anti-coagulated whole blood using a luminometer and luciferin/luciferase. The assay is used for the detection of cell-mediated immunity in an immunosuppressed population.

(PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K013169

Prescription Use ✓ OR Over-The-Counter Use _____
(Per 21 CFR 801.109)

(Optional Format 1-2-96)